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EXAMINER	
LAM, ANN Y	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 07/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/936,957	MEIKLE ET AL.	
	Examiner	Art Unit	
	Ann Y. Lam	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-6,8-12,15-20,36 and 39* is/are pending in the application.

4a) Of the above claim(s) *21-35,37 and 38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-6,8-12,15-20,36 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 5, 2006 has been entered.

As a preliminary matter, the Office notes that an advisory action was mailed out January 24, 2006, but that this advisory action should be disregarded. (Due to an internal error within the Office, the RCE was inadvertently missed and thus an advisory action was sent out instead of a regular first action on the merits.)

Status of Claims

Claims 2, 3, 7, 13 and 14 are canceled.

Claims 21-35 and 37 and 38 are withdrawn.

Claims 1, 4-6, 8-12, 15-20, 36 and 39 are currently pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 39 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 39 recites in line 19, "the lysosomal storage disorder listed in Table 2". The claim is indefinite in that it fails to point out what is included or excluded by the claim language. (Table 2 is not part of claim 36.) Thus, for examination purposes, the Office will interpret claim 36 to not be reciting any particular level of saposin.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1, 4, 15, 17, 18 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Brien et al. (1991), "Saposin proteins: structure, function, and role in human lysosomal disorders", THE FASEB JOURNAL, vol. 5(3), 301-8, in view of Sano et al., "Sphingolipid hydrolase activator proteins and their precursors", Biochemical and biophysical research communications, 165 (3), pp. 1191-7, 1989.

O'Brien teaches the invention substantially as claimed. More specifically, as to claims 1 and 39, O'Brien discloses the method of monitoring a lysosomal storage disorder in a patient (page 306, right column, lines 21-22), comprising: measuring the level of at least one saposin in a tissue sample of the patient (page 306, right column, lines 17-19),

comparing the first level to a baseline level, wherein the baseline level is the level of at least the first saposin as determined in a control population of patients unaffected by the lysosomal storage disorder (see page 307, description of figure 7, disclosing the amount of saposin in a control population, for a comparison allowing for a determination of deficiency of saposin in a sample population); and

determining a presence or extent of a lysosomal storage disorder when the first level is similar or different than the 95^{th} percentile of the baseline level of at least the first saposins in the control population (page 306, right column, third full paragraph, first sentence)

the similarity of the first level compared to the baseline level is an indicator of absence of the lysosomal storage disorder in the patient, and the difference of the first level compared to the baseline level is an indicator of presence or extent of the lysosomal storage disorder in the patient (page 306, right column, second full paragraph, and first sentence of third full paragraph);

and the saposin is selected from the group consisting of saposin A, B, C, D, and prosaposin (for example saposin A, page 306, right column, line 41.)

O'Brien teaches the detection of saposin, and its deficiency or accumulation, in specific tissue and cell samples as an indication of lysosomal storage disorder. However, O'Brien does not specifically teach detection of saposin in whole blood or plasma samples.

Sano teaches that saposin is not only found in tissues but is also found in human blood and plasma (see abstract.) It would have been obvious to one of ordinary skill in the at the time the invention was made to detect saposin in blood or plasma in the O'Brien method of detecting lysosomal storage disease, because Sano teaches that saposin is also found in blood and plasma and Sano teaches measuring levels of saposin in blood. Given the O'Brien teachings in comparing the levels of tissue saposin in a control population and in a sample population with lysosomal storage disorder and given that Sano teaches that saposin is also found in blood or plasma, one of ordinary skill in the art would have reasonable expectation of success for diagnosing or monitoring a lysosomal storage disorder using blood or plasma sample from a patient.

As to claims 4, 15, 17 and 18, O'Brien teaches the following limitations.

As to claim 4, O'Brien teaches indicating a presence of the lysosomal disorder when the first level exceeds the baseline level (page 306, right column, third full paragraph, first sentence.)

As to claim 15, the measuring step comprises detecting binding between a saposin polypeptide and an antibody (page 306, left column, lines 10-11.)

As to claim 17, the antibody is immobilized to a solid phase (page 306, right column, , line 18.)

As to claim 18, the lysosomal storage disorder is Niemann-Pick disease (page 306, right column, line 61.)

2. Claims 5, 6, 8-12, 19, 20 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Brien et al. (1991) Saposin proteins: structure, function, and role in human lysosomal disorders, THE FASEB JOURNAL, vol. 5(3), 301-8, in view of Sano et al., "Sphingolipid hydrolase activator proteins and their precursors", Biochemical and biophysical research communications, 165 (3), pp. 1191-7, 1989, and further in view of Dubensky et al., 6,376,236.

The method of O'Brien in view of Sano disclose the invention as claimed (see above). More specifically, O'Brien discloses the correlation between an accumulation of saposin and Gaucher's disease in patients, Gaucher's disease being a well known lysosomal disease.

However, neither O'Brien nor Sano specifically teach the step of monitoring the progression of the disease (claim 5), the patient undergoing treatment for the lysosomal storage disorder (claim 6), selecting a patient that is not known to have a lysosomal storage disorder before the measuring step; selecting a patient that is an infant (claim 9) or fetus (claim 10), (claim 11), nor the step of determining a treatment program (claims 19 and 20), nor the indication of positive treatment (claims 5, 11 and 12.)

Dubensky discloses a method of treating Gaucher's disease (col. 120, lines 33-59.)

As to claims 5, 6, 11, 12 and 36, it would have been obvious to measure the level of the saposin in a second tissue sample from the patient, the first and second samples being obtained at different times; and comparing the levels in the samples to indicate progression of the disease since Dubensky teaches that some lysosomal storage disorders can be responsive to treatment, thus teaching that after treatment, the disorder can be detected by the disclosed method to determine whether the disorder is responsive to the treatment. (As to claim 5, the saposin measured in a second tissue sample is deemed to be the second saposin in a second sample, as is claimed by Applicant.)

Similarly, as to claim 20, it would have been obvious to determine a treatment program based on the measurement since Dubensky teaches that some lysosomal storage disorders can be responsive to treatment, thus teaching that patients can undergo one of these treatments for lysosomal disorder.

Dubensky further teaches that Gaucher's disease affects infants and fetuses, as well as adults, (col. 120, lines 33-59.) It would have been obvious to one of ordinary skill in the art to use the method taught by O'Brien in view of Sano to detect Gaucher's disease in infants and fetuses that are not known to have Gaucher's disease, since Dubensky teaches that Gaucher's disease may affect infants and fetuses, (claims 8-10), as would be desirable for medical purposes. As to claim 19, it would have been obvious to one of ordinary skill in the art to inform the patient or a parent or guardian of an infant of the presence of the lysosomal storage disorder, as would be desirable to allow a patient or parent or guardian to permit treatment of the disease.

3. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over O'Brien, et al. (1991) Saposin proteins: structure, function, and role in human lysosomal disorders, THE FASEB JOURNAL, vol. 5(3), 301-8, in view of Sano et al., "Sphingolipid hydrolase activator proteins and their precursors", Biochemical and biophysical research communications, 165 (3), pp. 1191-7, 1989, as applied to claims 1 and 15, and further in view of Stastny, J., et al. (1992) Production and Characterization of a Monoclonal Antibody to Human Saposin C, HYBRIDOMA, vol. 11, 351-359.

O'Brien in view of Sano disclose the invention substantially as claimed (see above), except for the antibody being a monoclonal antibody.

Stastny discloses a monoclonal antibody (68-12) that reacts with saposin C. It would have been obvious to use this monoclonal antibody in the method taught by O'Brien in view of Sano in order to detect the level of saposin C because the high specificity of monoclonal antibodies for their corresponding antigen (in this case saposin C) would provide for a more sensitive assay for the detection of saposin C.

Response to Arguments

Applicant's arguments filed January 5, 2006 have been considered.

Regarding the 112, first and second paragraph rejections, these arguments are moot because these rejections have been withdrawn in view of the amendments to the claims. (A new rejection under 112, second paragraph of newly presented claim 39 has been made above however.)

Applicant's arguments regarding the 102 and 103 rejections however are not persuasive for the following reasons.

Applicant argues on page 7 that the O'Brien reference clearly demonstrates that three different tissues contain three different levels of saposin proteins and that no detectable levels of saposin A, B, C or D were found in the brains or livers of patients having Gaucher's disease, and that patients having Gaucher's disease had the highest spleen concentrations of saposin proteins when compared with the spleens from controls or all of the other LSD patients. Applicants submit that the knowledge of saposin proteins being found in blood, as indicated in the Sano reference, is not a critical link that would allow one of ordinary skill in the art to develop a diagnostic assay for an LSD (lysosomal storage disorder) based upon relative levels of saposin proteins in blood or plasma. Applicant states on page 8 that because the amount of saposin proteins can be variable in different tissues and in different LSD's conditions, it is unlikely that one of ordinary skill in the art would have been able to "predict" the alternating levels of the saposin proteins in plasma from control and LSD affected individuals. Applicant further notes on page 9 that the Sano reference does not indicate, suggest or even mention the levels of saposin proteins from LSD patients, and that neither the suggestion nor an expectation of successfully predicting that various saposin levels in blood or plasma show strong or weak correlations in patients having various LSD conditions can be found in the prior art.

These arguments are not persuasive because, as the Office has noted in the last Office action, O'Brien teaches determining the amount of saposin in a control population

and in a population known to have a lysosomal storage disorder and that a difference in saposin levels are found between the two groups (see page 307, brief description of figure 7, and page 306, lines 10-12 and first sentence of second full paragraph.) Given the O'Brien teachings of comparing the levels of tissue saposin in a control population and in a sample population known to have a lysosomal storage disorder in order to monitor a lysosomal storage disorder and given that Sano teaches that saposin is also found in blood or plasma, one of ordinary skill in the art would have reasonable expectation of success for diagnosing or monitoring a lysosomal storage disorder using blood or plasma sample from a patient. That is, given that O'Brien teaches an assay to detect saposin to monitor a lysosomal storage disorder and that the levels of saposin in patients with a lysosomal storage disorder is significantly different from those that do not have a lysosomal storage disorder, it would have been obvious to one of ordinary skill in the art to perform a similar assay to detect saposin in blood or serum, because Sano teaches that saposin is also found in blood or serum, to monitor a lysosomal storage disorder. Upon performing such an assay one of ordinary skill in the art would find the level of saposin in blood or serum of patients with LSD and in a control population that does not have LSD.

Applicant also argues on page 10 that while Patent '236 teaches a recombinant alphavirus particle that may help with the treatment of Gaucher's disease, the term "saposin" is not even used through the document and there is no mentioning of utilizing or correlating blood or plasma saposin proteins to diagnose or monitor an LSD. These arguments are not persuasive because Patent '236 is relied upon by the Office for its

teaching that treatment is known for Gaucher's disease, not for any teaching of saposins, because that is taught by O'Brien, as indicated in the above rejections.

Applicant also submits on page 10 that the combined teachings of O'Brien and Sano do not suggest a reasonable expectation of success for diagnosing or monitoring LSD using blood or plasma from a patient, and that data of saposin levels obtained with brain, liver and spleen cannot be extrapolated to blood. These arguments are not persuasive because the grounds of rejection are not based upon extrapolating data of saposin levels obtained with brain, liver and spleen to blood. Rather, they are based on the teachings of O'Brien that patients with a lysosomal storage disorder will present a level of saposin that is significantly different from those that do not have a lysosomal storage disorder, and comparing the levels of tissue saposin in a control population and in a sample population with lysosomal storage disorder for monitoring lysosomal storage disorder. Given Sano teach that saposin is also known to be found in blood or plasma, one of ordinary skill in the art would recognize that a similar assay may be performed on the level of saposin in blood or serum for diagnostic purposes, as indicated in the above rejections. Upon such an assay one of ordinary skill in the art would find the level of saposin in blood or serum of patients with LSD and in a control population that does not have LSD.

Applicant also argues on page 12, that the teachings of O'Brien show that the level of saposin A varies dramatically in brain, liver and spleen from patients having Sandhoff disease. Applicant asks on page 13 how would one of ordinary skill in the art have a reasonable expectation of success of diagnosing or monitoring a lysosomal

storage disorder with liver samples from a patient, using brain and spleen data? In response, the Office again notes that the grounds of rejection are not based upon extrapolating data of saposin levels, in this case, from brain and spleen to liver. Rather the grounds of rejections are based on the obviousness of performing an assay on a patient and on a control population using blood samples, as mentioned earlier. Upon such an assay one of ordinary skill in the art would find the level of saposin in blood or serum of patients with LSD and in a control population that does not have LSD.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

6/25/06

Ann Lam